CASE REPORTS

Carbon Tetrachloride Intoxication

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CARBON tetrachloride damages the kidneys and liver in a characteristic manner which is not as well recognized clinically as it might be. The following report of a patient who recovered after drinking carbon tetrachloride demonstrates the resulting disturbances of renal and hepatic function.

CASE REPORT

A 34-year-old white housewife entered the hospital May 14, 1949, with complaint of icterus for 24 hours and emesis for one week.

For five years prior to 1946 the patient had consumed alcohol in "small amounts" with food. In 1946 she began periodically to drink heavily, consuming one pint of whiskey daily at intervals for about one year. In January 1949 she again began to drink heavily and this continued to the present illness. For several days prior to the week preceding hospitalization she had been drinking large amounts of whiskey. When, seven days before hospitalization, no more whiskey was available in the house, she drank an unspecified amount of household ammonia and 3 ounces of rubbing alcohol.

During the following week she ate almost nothing, vomited often, passed dark to black stools, and had generalized upper abdominal pain. At the end of this week she vomited blood and noted epistaxis. The urinary output had been scant all week but was not carefully observed. When jaundice was noted medical care was sought and the patient was immediately hospitalized.

The past history was essentially unimportant. The husband and two children, ages 6 years and 18 months, were living. Pregnancies had been uneventful. Blood pressure and urinalysis in July 1947 were "normal." Blood pressure at term in January 1948 was 150 mm. of mercury systolic and 90 mm. diastolic, and urine at that time contained a faint trace of albumin. Physicians had often noted an irregularity of the heartbeat but there was no known rheumatic fever and no symptoms indicative of heart or lung disease. Menstrual history was normal with menarche at age of 14. There were no past symptoms referable to the gastrointestinal or genitourinary tracts.

Upon physical examination at the time of admission to the hospital, the patient was noted to be well developed, well nourished, drowsy, and depressed. She was moderately icteric and had fetor oris. No spider angiomata were noted. The respirations were 20 per minute and regular. The pulse rate was 84 per minute and the rhythm was regular. Blood pressure was 134 mm. of mercury systolic and 70 mm. diastolic. The temperature was 98.6° F. Blood was oozing from the nose. Pupillary reactions and extraocular movements were normal, and no abnormality was noted in the ocular fundi. The sclerae were yellow. The tongue was coated and dry, teeth were clean, and the pharynx was not injected. There was no enlargement of lymph nodes. The thyroid gland was not enlarged and there was no venous distention. The neck was supple, and the trachea was in the midline. The lungs were clear to percussion and auscultation, and the breasts were normal. The apparent heart size was not increased and there was a Grade II systolic murmur, loudest at the apex, but heard over the entire precordium. The abdomen was soft and muscles flabby. The liver edge, which was palpable on expiration 3 cm. below the right costal margin in the midclavicular line, disappeared below the sternum in the midline. It was sharp, irregular and tender. Spleen and kidneys were not palpable. No other masses or tenderness were noted. There was no evidence of fluid in the abdomen. No abnormalities were observed in the extremities. Good peripheral pulsation was noted and normal tendon reflexes were elicited. The cervix, corpus uteri and adnexae were normal.

Course in Hospital: At the time of admission to the hospital the diagnosis was alcoholic cirrhosis of the liver with recent exacerbation. The specific gravity of a specimen of voided urine was 1.006, which was significant because of the dehydration. (The correct diagnosis could have been made at this point, but was not.) The reaction was acid and the urine contained 1-plus protein and occasional erythrocytes and leukocytes, but no casts. Vitamin K (72 mg.) was given intravenously and the epistaxis stopped. Because of vomiting, parenteral feeding was necessary on both the first and second hospital days (Chart 1). No electrolytes were given. Urinary output of 700 cc. seemed compatible with dehydration, but because of persistent drowsiness, further chemical studies were ordered.

On the third hospital day (tenth day of illness) the patient was both restless and drowsy, had dark fluid stools and emesis. Demerol® was given for relief of pain. Parenteral feeding again was carried out (Chart 1) and Vitamin K was given. The urine output was 900 cc. and the general picture was still in keeping with the diagnosis of dehydration and severe hepatitis. Later that day, however, the laboratory reports were as shown in Chart 2 (tenth day).

It was then evident that the patient had renal as well as hepatic disease and a search for toxic agents was made. It was known that the patient had ingested household ammonia which is not harmful. The rubbing alcohol which she had consumed contained: ethyl alcohol 70 per cent, acetone approximately 8 per cent, methyl-iso-butylketone approximately 1.5 per cent, and a small amount of sucrose-octa-acetate for bitter taste. None of these agents is known to have such toxic effects.

A partially filled bottle of "Energine Cleaning Fluid, Fireproof" was found in the patient's home and she admitted

From the Cedars of Lebanon Hospital, Los Angeles.

CHART 1.—*Treatment*

	Day of Illness																			
	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27
Intravenous fluid (cc.)	1,000	2,000	2,000	2,500	2,000	2,000	1,600	1,670	1,550	1,650	....	....	....	....	....	....	....	....	....	....
Sodium chloride (gm.)	0	1.0	1.0	9.5	18	9.0	0	0	1.0	1.0	....	....	....	....	....	....	....	....	....	....
Carbohydrate (gm.)	50	50	50	100	100	50	50	50	....	....	....	....	....	....	....	....	....	....	....	....
Protein (gm.)	0	50	50	25	0	0	0	0	50	50	....	....	....	....	....	....	....	....	....	....
Ringer's lactate (cc.)	0	0	0	1,000	0	1,000	0	0	....	....	....	....	....	....	....	....	....	....	....	....
Vitamin B complex (ampules*)	1	1	1	1	0	1	1	1	....	....	....	....	....	....	....	....	....	....	....	....
Vitamin K intravenously (mg.)	72	0	72	0	72	0	72	0	72	0	72	....	....	....	....	....	....	....	....	....
Vitamin K orally (mg.)	....	....	....	....	....	....	....	....	....	....	30	30	30	30	30	30	30	30	30	30
Blood (cc.)	0	0	0	0	0	1,000	500	500	....	....	....	....	....	....	....	....	....	....	....	....
Liver extract (units)	....	....	....	....	....	....	....	15	15	....	15	....	15	....	15	....	15	....	15	....
Choline (gm.)	....	....	....	....	....	....	....	....	....	....	....	4	4	4	4	4	4	4	4	4

*Each ampule contained: Thiamine hydrochloride, 10 mg.; riboflavin, 10 mg.; ascorbic acid, 100 mg.; pyridoxine hydrochloride, 5 mg.; calcium pantothenate, 50 mg.; nicotinamide, 250 mg.

CHART 2.—*Results of Laboratory Tests*

	Day of Illness															3 Mos. Later
	8	9	10	11	12	13	14	15	16	17	18	19	21	25	26	
Urine volume (cc.)	250	700	900	650	250	1,000	2,080	2,480	3,950	1,400	....	....	....	....	....	....
Nonprotein nitrogen (mg. per 100 cc.)	....	....	232	246	208	221	....	....	....	....	....	....	....	47	....	42
Creatinine (mg. per 100 cc.)	....	....	12.1	....	16.9	15.2	14.5	13.2	....	....	....	10	....	....	1.75	....
Carbon dioxide combining power (volume, per cent)	....	....	....	27	....	....	31	....	....	....	....	....	....	....	....	....
Serum chloride as NaCl (mg. per 100 cc.)	....	....	....	380	407	480	475	....	....	....	....	....	....	....	....	....
Serum potassium (mg. per 100 cc.)	....	....	....	....	....	....	20	....	....	....	....	....	....	....	....	....
Serum calcium (mg. per 100 cc.)	....	....	....	....	....	....	....	10.7	....	....	....	....	....	....	....	....
Leukocytes per cu. mm. (with percentage of polymorphonuclear cells shown in parentheses)	....	....	15,300 (p. 81)	....	....	16,600 (p. 90)	....	20,500 (p. 87)	....	....	19,800 (p. 76)	....	17,100 (p. 77)	11,100 (p. 73)	....	7,100 (p. 55)
Hemoglobin (gm. per 100 cc.)	....	....	11.2	....	....	7.1	....	10.7	....	....	13.3	....	....	12.7	....	12.5
Prothrombin (per cent of normal)	....	....	72	....	....	....	38	92	....	....	80	....	....	61	....	90
Albumin-globulin (gm. per 100 cc.)	....	....	3.7/2.2	....	....	....	....	....	....	4.5/2.5	....	....	....	....	....	....
Icteric index (units)	....	....	35	....	40	....	....	....	....	....	31	....	....	9.5	....	10
Cephalin flocculation (units)	....	....	3+ (24 and 48 hrs.)	....	....	....	....	....	....	....	....	....	....	Neg. 48 hrs.	....	....
Cholesterol-ester (mg. per 100 cc.)	....	....	....	153/33 =21%	....	....	....	....	....	....	....	....	....	270/187 =70%	....	301/260 =86%
Carbohydrate (mg. per 100 cc.)	....	....	....	117	....	....	....	....	....	....	....	....	....	....	....	....
Thymol turbidity (units)	....	....	5.2	....	....	....	....	....	....	....	....	....	....	....	....	....

Blood type "O", Rh+.

having drunk about two ounces of this ten days previously. This fluid contains 75 per cent carbon tetrachloride and 25 per cent naphtha by volume, and this fact confirmed what had become a strong suspicion of carbon tetrachloride intoxication.

On the 11th day the blood pressure was 150 mm. of mercury systolic and 60 mm. diastolic. There was a sinus rhythm with a pulse of 90 and temperature was 98.6° F. Edema of the face and back had developed and what one observer thought were spider angiomata were noted on the nose. No change in the liver was noted upon physical examination. The urinary output was 650 cc. in 24 hours. The serum chlorides were 380 mg. per 100 cc., so despite the presence of edema the patient was given 1 liter of 5 per cent glucose in Ringer lactate solution (containing 9 gm. sodium chloride) and 1 liter of 5 per cent glucose in water intravenously. In more detailed examination of the urine on this day, the following data (calculated on the basis of 24-hour urine excretion) were noted: Protein, 0.968 gm.; sodium chloride, 1.30 gm.; leukocytes, 36,000,000; erythrocytes, 60,000,000; casts (broad), 100,000.

On the 12th day the blood pressure was 160 mm. of mercury systolic and 60 mm. diastolic and the face was edematous. The abdomen was distended and the patient had black, liquid stools and bloody vomitus. Vitamin K again was given intravenously but severe nosebleed developed and blood and clots were "vomited." A large clot was noted in the nasopharynx, and there was active bleeding in the left naris. After the mucosa had been shrunk and old clots removed, no active bleeding point could be seen. A small ulcerated area was noted in the middle of the left septum, and the right middle turbinate appeared ecchymotic. There was no further bleeding. The pulse rate remained between 80 and 90 and the blood pressure did not fall so that the blood loss was thought to be unimportant. The urine was alkaline with a specific gravity of 1.010, and albumin 1-plus. There were three to four leukocytes and triple phosphate crystals per high power field. Because serum chlorides were still low (407 mg. per 100 cc.) the patient received 2 liters of 5 per cent glucose in normal saline by vein but excreted only 300 cc. of urine. The nonprotein nitrogen level fell but the creatinine rose (Chart 2).

On the 13th day there was no new bleeding but dark liquid stools were again noted. The blood pressure was 150 mm. of mercury systolic and 60 mm. diastolic and the pulse rate was 84, but as the hemoglobin content of the blood was 7.1 gm. per 100 cc., the patient was given 1,000 cc. of whole blood plus 1 liter of 5 per cent glucose in Ringer lactate solution (containing 9 gm. sodium chloride). The urine remained alkaline and the serum chlorides rose. The nonprotein nitrogen rose slightly but the creatinine fell. Urinary output was 1,000 cc.

On the 14th day the patient received an additional 500 cc. of whole blood plus vitamin K intravenously. Output of urine was more than 2,000 cc. The creatinine continued to fall and serum chlorides remained high but it was not until the 15th day that the patient showed clinical improvement; she was less nauseated and more alert and became interested in getting well. The blood pressure was 190 mm. of mercury systolic and 90 mm. diastolic. A few rales were noted at both lung bases. The creatinine content of the blood fell further and the hemoglobin value rose. The patient voided 2,500 cc. of urine. An additional 500 cc. of whole blood plus 1 liter of 5 per cent glucose in water was given.

On the 16th and 17th days proteins were given intravenously, and after that the patient was able to take nourishment by mouth. The remainder of the treatment is shown in the charts.

On the 22nd day blood pressure was 160 mm. of mercury systolic and 90 diastolic with a constant trigeminal rhythm. A soft systolic murmur was heard at the apex. The lungs were entirely clear. The abdomen was soft, and the spleen and kidneys were not palpable. The liver was 3 cm. below the right costal border on expiration and extended across the midline into the epigastrium with a sharp, non-tender edge. There was no icterus. Three days later, on the 25th day, blood pressure was 170 mm. of mercury systolic and 90 diastolic.

Results of urinalyses between the 17th and 25th days were: Specific gravity, from 1.001 to 1.009; reaction, neutral to alkaline; albumin, zero to 2-plus; leukocytes per high power field, 2 to many, and erythrocytes, 2 to 3. No casts were noted.

An electrocardiogram taken on the 22nd day showed sinus rhythm, rate 90, ventricular premature complexes occurring regularly every third beat, and inversion of T-2 and T-3. Subsequent electrocardiograms, taken two weeks and again two months later, showed T-2 upright, T-3 and P-3 inverted. The ventricular premature complexes remained but were less regular.

Upon subsequent examination two months after the patient had left the hospital and resumed moderate activity, there was a 4-pound gain in weight, blood pressure was 130 mm. of mercury systolic and 80 diastolic, trigeminal to bigeminal rhythm becoming regular after mild exercise, a softer systolic apical murmur, and a barely palpable non-tender liver edge.

Results of laboratory work not shown in Chart 2 but done three months after discharge from the hospital follow: Bromsulfalein test, no dye in serum after 45 minutes; erythrocytes, 3,940,000 per cu. mm. of blood; phenolsulfonphthalein excretion; 54.4 per cent in 2 hours after intramuscular administration of dye; Mosenthal test, concentrated specific gravity 1.017, diluted specific gravity 1.002; urine contained no albumin and 2 to 5 leukocytes per high power field; blood sedimentation rate, 46 mm. in one hour.

DISCUSSION

Most reported cases of carbon tetrachloride poisoning result from inhalation of vapors. Carbon tetrachloride, whether inhaled as fumes or ingested as liquid, characteristically damages the liver and kidneys. Whether or not the injury will be fatal depends primarily on the dose. Alcohol ingestion predisposes to more serious damage. Supposedly the liver is more severely damaged after ingestion of carbon tetrachloride and the kidneys are more severely damaged after inhalation.[2, 4, 5, 8, 9]

The renal disturbance is toxic nephrosis with damage primarily occurring in the epithelium of the distal tubules. Complete recovery occurs if the patient survives. The hepatic disturbance is essentially central necrosis of the lobule, with recovery if the patient survives.[1, 6, 7, 10]

The patient in the case here reported was not severely oliguric during the period of observation. There were relatively few casts and cells and relatively little protein in the urine, and the blood pressure was only moderately elevated. Yet edema was present and there was severe nitrogen retention and the content of chlorides in the serum and urine was low, indicating pronounced renal disturbance. Therefore the problem of whether or not to give sodium chloride was confronted. There is nothing definitive on this point in the literature, but most recent investigators would withhold salt in the presence of edema.[3, 6] The patient in the present case received 9 gm. of sodium chloride on the 11th day, 18 gm. on the 12th day and 9 gm. on the 13th day. Diuresis began on the 13th day.

The liver was badly damaged, as was indicated clinically by enlargement, tenderness, jaundice and hemorrhage. The

low cholesterol and esters, prothrombin disturbance and results of a cephalin flocculation test gave laboratory confirmation. The normal serum protein level illustrated the well-known fact that liver function may be differentially disturbed. The bleeding which was present was probably associated with the demonstrated prolongation of prothrombin time but cannot be more fully explained until knowledge of the entire prothrombin mechanism is more complete. Platelets and capillary fragility were normal.

The damaged liver needed protein as well as carbohydrate for regeneration and the patient received intravenous protein until the threat of death from kidney failure seemed more imminent than the threat of death from hepatic failure. No protein was given from that time (12th day) until there was evidence of kidney recovery (16th day). The transfused blood, which was given primarily to counteract the hemorrhage, may well have been an important factor in aiding renal recovery (the urinary output was greater the day preceding the hemorrhage than on the day of the hemorrhage and then increased greatly after blood was given).

In evaluating the effect of the treatment, it must be recognized that the patient was not observed by a physician until seven days after ingestion of the carbon tetrachloride. This perhaps indicates that under-treatment is of some value as contrasted to the temptation to do too much. The determining factor as to eventual outcome is the severity of the damage done to the liver and kidneys, and treatment is aimed at maintaining the body economy during the temporary illness of these vital organs. Administration of too much fluid and electrolyte cannot force the kidneys to function, but can drown the patient.

SUMMARY

A patient drank less than 6 ounces (the exact amount is not known) of a solution containing 75 per cent carbon tetrachloride. Nausea, vomiting and abdominal pain developed immediately. Subsequently jaundice, hypoprothrombinemia, and hemorrhage developed, and results of laboratory tests were indicative of liver damage. Oliguria, edema, azotemia, mild hypertension, hypochloremia, and acidosis due to kidney damage also developed.

Treatment consisted of cautious administration of moderate amounts of fluid and carbohydrates; sodium chloride was given when the serum chlorides were low; very little protein was given because of severity of the renal disturbances. Vitamin K and whole blood were also given. The patient recovered.

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The Significance of Pure Pigment Calculi in Biliary Operations

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PIGMENT calculi in the biliary tract indicate an underlying hemolytic process. This process may be either familial or acquired hemolytic jaundice. Familial hemolytic jaundice has long been regarded as an entity apart from the acquired type. The familial type, first described in 1900 by Minkowski, is characterized by the presence of spherocytic erythrocytes in the circulating blood associated with increased fragility of the red cells. In the acquired type, first described by Hayem and by Widal, spherocytes are usually absent, reaction to Coomb's test is positive, and there is frequently a history of exposure to a hemolytic agent. The following case does not fit exactly into either category.

CASE REPORT

A 22-year-old white female had sudden onset of severe colicky pain in the right upper quadrant of the abdomen and radiating to the region of the right scapula. A few hours later nausea and vomiting began and 30 hours later generalized jaundice developed. The jaundice and pain in the right upper abdominal quadrant continued in varying degrees for three weeks.

At the age of 13 the patient had had jaundice associated with an enlargement of the spleen. A diagnosis of catarrhal jaundice was made at that time. At the age of 15 years she was found to have an enlargement of the spleen, associated with moderate anemia. At that time, erythrocytes numbered 2,500,000 per cu. mm. of blood. At the age of 19 years she was kicked on the upper abdomen by a horse. Because of the possibility of injury to an intra-abdominal viscus, exploratory laparotomy was performed. No ruptures were noted in the viscera, but there was a retroperitoneal hematoma. From that time until the present illness, splenic enlargement associated with anemia had been noted in periodic physical examinations. There was no history of drug idiosyncrasy or of the ingestion of drugs other than preparations of liver and vitamin B complex.